

REMARKS

The specification has been amended to reflect the national stage status.

In addition, the specification and claims have been amended according to amendments effected to the international application. These amendments were filed on July 17, 2001 and October 3, 2001 and were annexed to the International Preliminary Examination Report. An English translation of the cover letters for these amendments are also submitted herewith for the information of the Examiner.

Attached hereto is a marked-up version of the changes made to the specification by the current amendment. The attached page is captioned "Version with markings to show changes made".

Favorable action on the merits is solicited.

Respectfully submitted,

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DESCRIPTION**Biarylurea Derivatives**

and
of this application is a 371 of PCT/JP00/04991 filed July 26, 2000.

5 Technical Field

The present invention relates to biarylurea derivatives di-substituted with aromatic ring or heteroaromatic ring, which are useful as pharmaceutical composition, and to the production method and use thereof.

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Background Art

In the growth of the normal cells, cell division and its pause occur orderly according to the cell cycle, on the contrary, the growth of cancer cells is characterized by 15 its disorderedness, thus the abnormality in the cell-cycle regulating system is presumed to be directly related to the oncogenesis and malignant degeneration of cancer. The cell cycle of mammalian cells is controlled by a group of serine/threonine kinase called as cyclin dependent kinase 20 (hereinafter denoted as "Cdk") family. Cdk needs to form a complex with a regulatory subunit called cyclin, in order to exhibit its enzyme activity. Cyclins also have a family. Each Cdk molecule of which is considered to regulate 25 progression at a specific stage of the cell cycle by forming a complex with the specific cyclin molecule which is expressed at the corresponding stage of the cell cycle. For example, D-type cyclin regulates the progression of G1 phase by binding to Cdk4 or Cdk6, and cyclin E-Cdk2 regulates the progression of G1/S boundary, cyclin A-Cdk2